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Survey of Mechanisms in Electrochemical Treatment (ECT) of Cancer

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INTRODUCTION

The first attempt to utilise the system of biologically closed electric circuits (BCEC) (9) with the aim to treat cancer was performed as an activation of the vascular-interstitial closed circuit (VICC). These treatments are called electrochemical treatments (ECT) because they are not exclusively the result of the so-called contact current of Galvani (and Volta), induction current of Faraday, or displacement current of Maxwell. Evidently, none of these scientists could have had any idea about the complex BCEC-system which makes biological matter capable of utilising electricity for structural developments and functions. ECT of cancer therefore includes galvanic, faradic, and displacement current, which are all part of ELECTRICITY, as well as the sequences of electrochemical events and transports which occur at the interactions between the electric and magnetic fields with the biological substrate in the BCEC; the electrochemical system of the body.

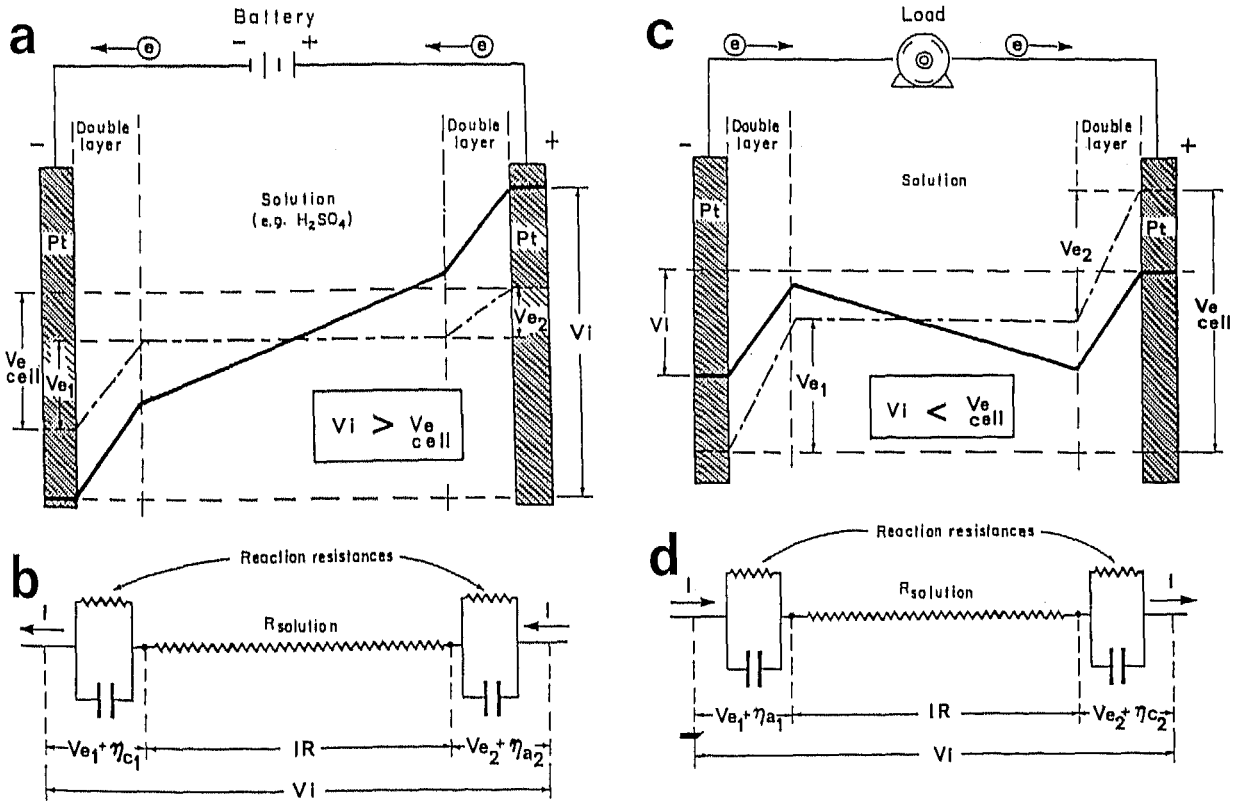

Fig. 1. (*a*) A driven cell, corresponding to Phase I in ECT. Two platinum electrodes are here immersed in an electrolyte (e.g. H_2SO_4). By increasing the voltage from zero, current starts to flow at equilibrium voltage. Above that level an overvoltage will drive current leading to electrode-electrolyte reactions and transports. In ECT, "distant field effects" also take place in the tissues. (*c*) A selfdriving cell, corresponding to Phase II in ECT. The direction of current is opposite to that in the driven cell, if the battery in (*a*) is replaced by a load or the electrodes are shortcircuited. An open circuit between the electrodes during Phase II gives a modified reversal of current in the tissues over multiple BCEC systems, which contain redox proteins in cellular walls serving as reversible electrodes. (*b*) and (*d*) are analogues.

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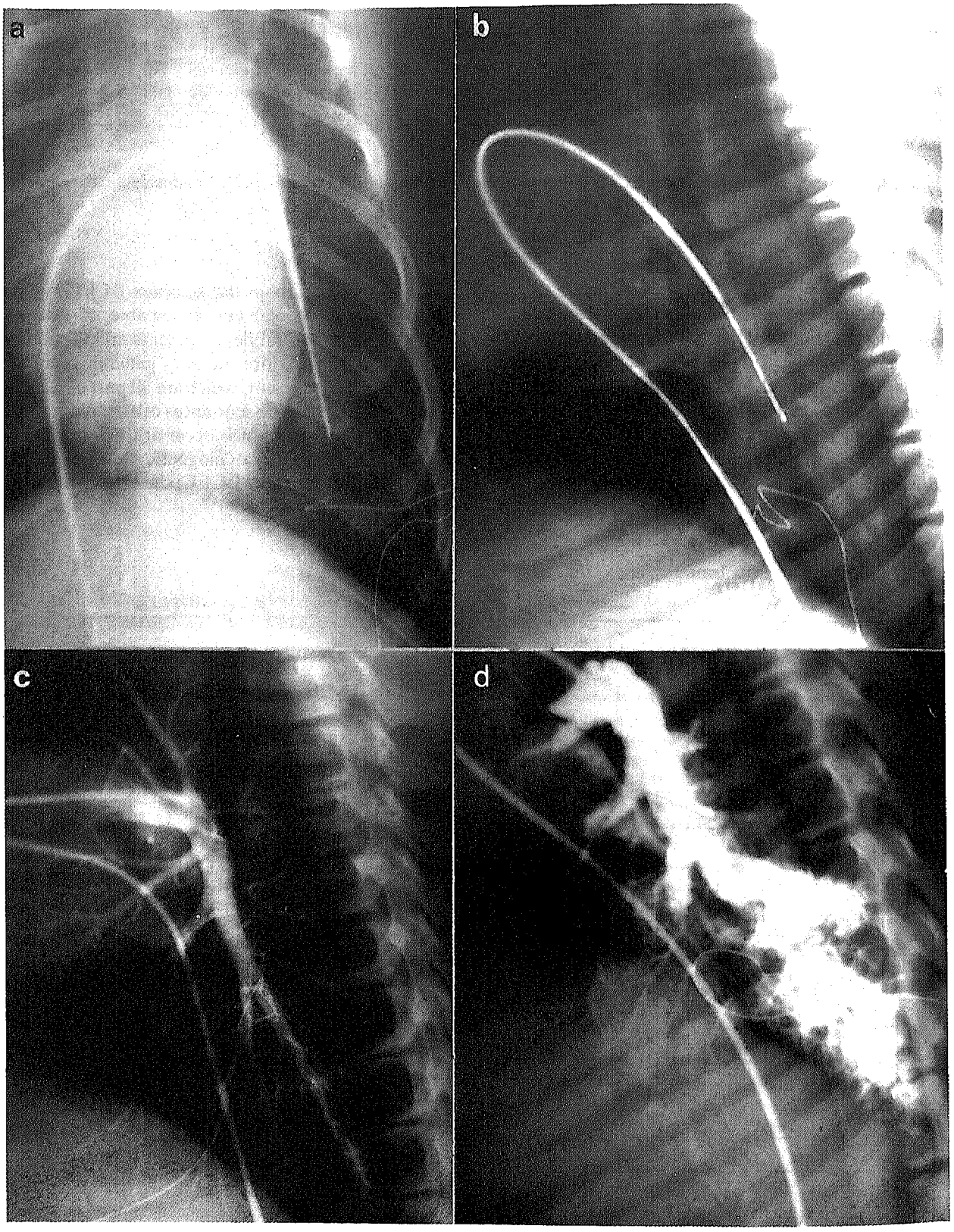


Fig. 2. Dog in general anaesthesia. The catheter in v. femoralis to the left pulmonary artery has a stainless steel guidewire serving as cathode. A platinum string electrode is percutaneously inserted into the left lower lobe. (*a*) Frontal, (*b*) lateral view. (*c*) Preliminary angiogram with Urografin shows patent normal pulmonary arteries. (*d*) Angiogram after 180 C at 20 V. The pencil-large arteries in the electronegative field are funnel-shaped and blocked by compression by electro-osmotic tissue water. Extravasation of contrast material occurs in the anodic field.

ECT represents basically an *in vivo* electrophoretic treatment which is entirely different from currently practiced conventional treatments of cancer.

ECT consists of two phases, the charging (Phase I) and the discharging (Phase II) of an electrophoretic process.

In Fig. 1*a* and *c* the function of an electrochemical cell is presented, partly after Bockris and Drazic (1). It illustrates the technical correspondence with Phases I and II in ECT. Fig. 1*b* and *d* are analogous to *a* and *c*.

The cell in Fig. 1*a* is driven (charged) by an external source of power with the anode (+) and cathode (−), representing platinum electrodes in contact with the electrolyte (here $H_2SO_4 + H_2O$). Electrons flow in the metallic parts and ions in the electrolyte. At low voltage, no current flows in the circuit. The reason is that the electrode-electrolyte interphases present resistances together with other resistances of the circuit which have to be overcome. By gradually increasing the voltage applied to the electrodes, current starts to flow at a certain voltage, which occurs above the so-called equilibrium voltage. The magnitude of voltage difference applied above the equilibrium voltage will drive the circuit and is called the overpotential. At the transfer of electrons, which then occurs across the electrode-electrolyte interphases, many effects take place with formation of anodic and cathodic products of reaction. The development of products of reaction and flow of ions when current drives the process corresponds to the charging of an electrophoretic cell (polarisation of the system, Fig. 1*a*).

When the external source of power has polarised the cell and is replaced by a load, or the cables are shortcircuited, a selfdriving system is created. This means that current will flow in the reverse direction and the cell is discharged (Fig. 1*c*). Correspondingly, when current is driven between electrodes in tissue which is conductive for ions, the electrophoretic ECT system will become polarised (Phase I). When removing the driving source of power, or when for instance shortcircuiting, the ECT system will also become selfdriving with reversal of the current (Phase II). Interestingly enough, biological tissue seems to be capable of reversing current without the presence of metal electrodes or for instance a shortcircuiting of their cables. This is possible because of the multiple biologically closed electric circuits (BCEC systems [9, Chapter XII]) in tissues, which also contain redox-enzymes serving as reversible electrodes (9, pp. 144–154).

DEMONSTRATION OF ECT EFFECTS

The close-contact effects at the electrodes in the lung of a dog are shown in Fig. 2. A stainless steel electrode is inserted via a catheter into the pulmonary artery and made electronegative, and a platinum string electrode is percutaneously inserted into the pulmonary tissue and made electropositive (Fig. 2*a* and *b*). A pulmonary angiogram shows the pulmonary vessels before (Fig. 2*c*) and after delivery of 180 coulomb (C) of DC current at 20 V (Fig. 2*d*). By comparison, we can see multiple funnel-shaped blockings of pulmonary artery branches in the cathodic field after the flow of current, and an extravasation of the contrast material (Urografin) in the anodic field of the lung. The funnel-shaped blockings of the vessels in the cathodic area are due to an increase of turgor pressure caused by electro-osmotic flow of tissue water (9, pp. 135, 199, 322, 323) from the anodic to the cathodic part of the field. These narrowings represent one of the exceedingly important distant field effects between the electrodes.

The reactions at the contact of the electrode-electrolyte leading to polarization are apparent (Phase I). In Fig. 3 the lung of the dog is seen sectioned. Hydrolysis (decomposition of water) leads to anodic acidity (H^+), pH 2 and cathodic alcalinity (OH^-) pH 12. These compounds and particularly H^+ destroy tissue around the electrodes. The black anodic area in the lung is formed by acidic haematin, which is derived from extravasation of the blood and its transformation by protons. Similarly, dark base haematin is formed in the cathodic area by OH^- ions. The sectioned lung also shows a dry anodic and a wet cathodic field-area which correspond to the electro-osmotic transport of water. The white centre of the

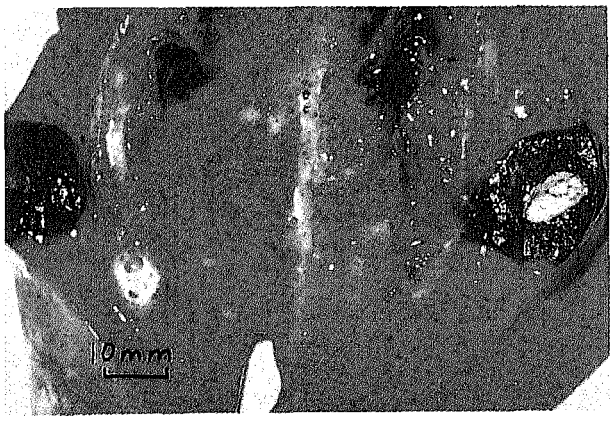


Fig. 3. The "killing effect" of H^+ ions evolved from hydrolysis transforms diapedetic blood into acidic haematin (black). The central white area is formed by Cl_2-bleaching the haematin. The anodic area is black and dry. The cathode is dark by base haematin and wet by electro-osmotic tissue water from the anodic field.

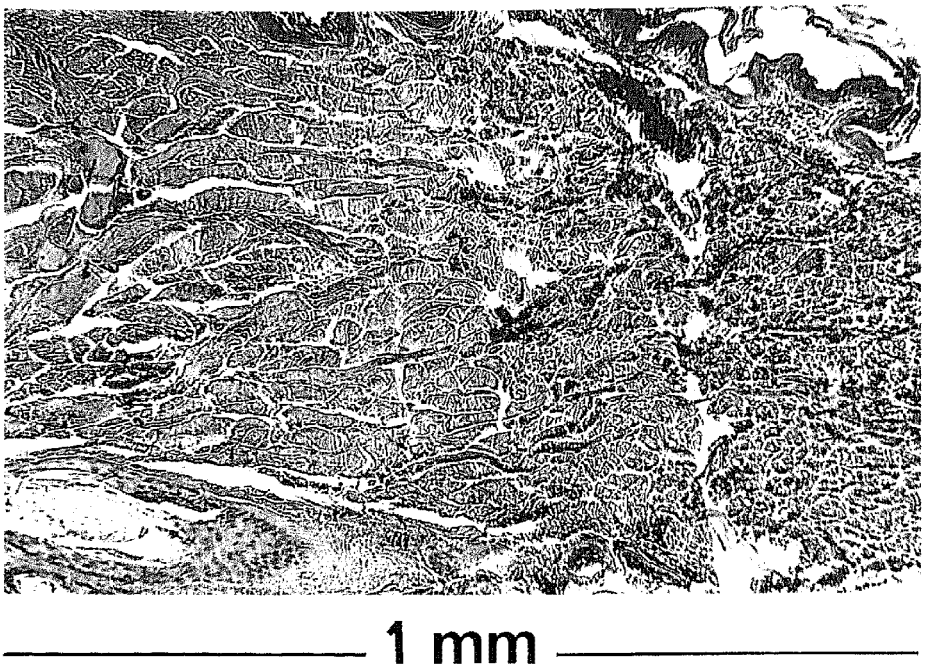


Fig. 4. Anodic destruction in muscle of the back of a dog. H^+ diffusion and migration are counteracted by the buffering capacity of tissue fluid which makes the border of the injured tissue very sharp.

acidic black area is due to the bleaching by Cl_2. It represents a small central position, as the relatively large Cl_2 molecules without carrying any excess of charge cannot compete with the destructive effect of H^+ ions. Protons easily diffuse and migrate more rapidly in the anodic field than any other ions. Their effects on tissue is counteracted by the buffering capacity of the tissue fields, which explains the very steep boundary gradient of the protons, diffusing and migrating in muscle tissue, as seen in Fig. 4.

Besides anodic Cl_2 and O_2 gas, cathodic H_2 gas is also formed. The gaseous materials elevate the pressure in the tissue and produce interference with the tissue circulation and the electrode-electrolyte reactions. They form anodic (Fig. 5*a*) and cathodic (Fig. 5*b*) gas bubbles. The electric fields induce a charge-displacement in these dielectric materials with secondary gas adsorption onto the electrodes. Small gas bubbles are also "pumped" out into the tissue by gas pressure, and in the anodic field, close to the electrode, also into intercellular spaces by dielectrophoresis.

The result of polarisation during Phase I can be analysed by electrochemical recordings (Fig. 6*a*) after termination of the Phase I reactions produced on a filter soaked in litmus-NaCl-water. The tracing shown in Fig. 6*b* is made with a platinum electrode in relation to the reference (RE) and moved along the filter from left to right and then back again. A voltage difference is recorded between cathode (Ec) and anode (Ea) and the tracing is superimposed by outward decreasing anodic and larger cathodic oscillations. These are

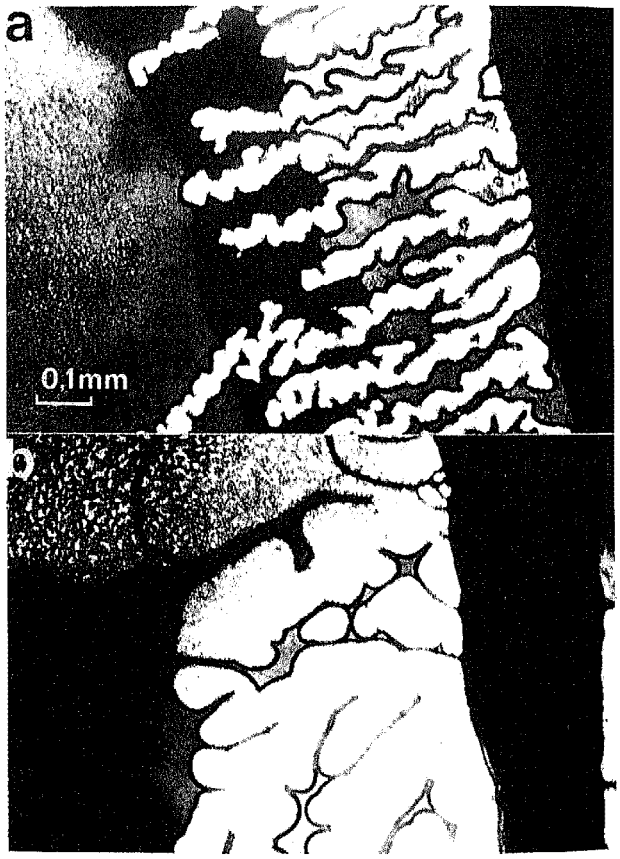


Fig. 5. (*a*) From hydrolysis of water and electronation of cathodic $H^+ + H^+ \rightarrow H_2$ = hydrogen gas is formed as bubbles. (*b*) Anodic bubbles of Cl_2 and O_2. The gas bubbles are attracted to the cathodic and anodic electrodes by dipole induction. They grow outward as "dendrites" and give off bubbles of gas into the surrounding tissue. The formation of gas disturbs the electrode-electrolyte reactions.

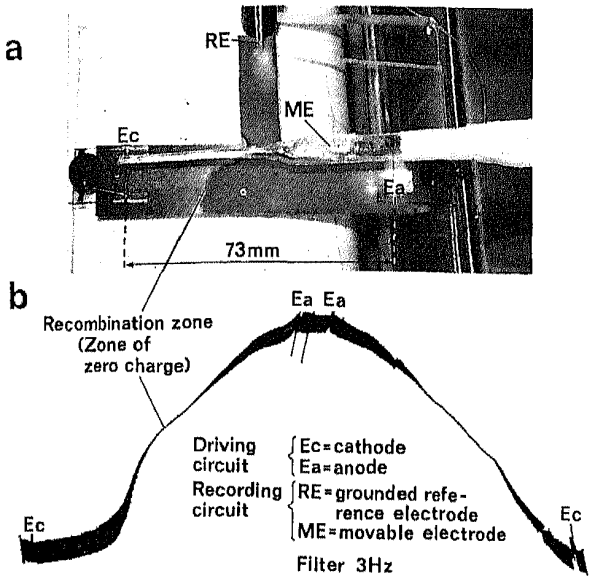


Fig. 6. (*a*) The products of electrode-electrolyte ($NaCl + H_2O$) reactions with platinum electrodes show blue cathodic and red anodic litmus reactions. When they meet cathodic OH^- and anodic H^+ they recombine to water. Some bleaching is seen close to the electrode by Cl_2 gas. (*b*) Voltage difference is recorded by non-polarisable $Ag–AgCl_2$ electrodes in KCl bridges. When the ME electrode is moved over the filter paper from Ec (cathode) to Ea (anode) and then back, the recording shows rapid oscillations by nonvisible gas into the filter paper. They reach a minimum at the zone of recombination of OH^- and H^+ ions. Gas bubbles leaving the electrodes fluctuate the current, which in a patient can produce pain.

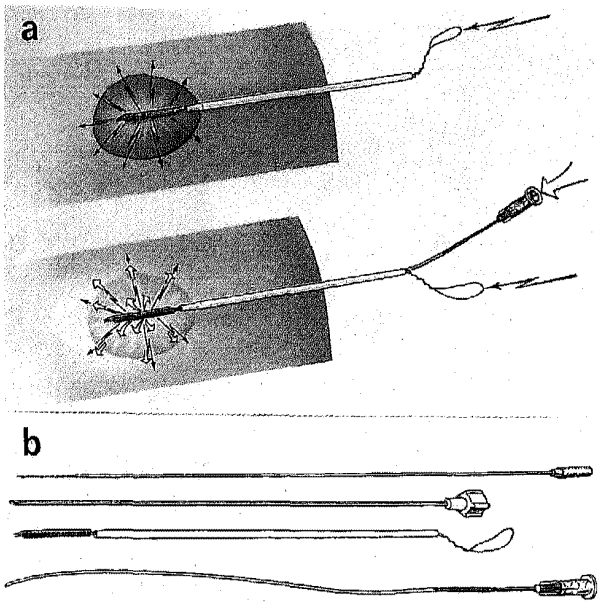


Fig. 7. (*a*) By using a perfusable electrode such as the Superflux electrode® which is built as a coil of platinum thread it is possible to suck out gas or to flush the electrode canal with saline solution or to add a chemotherapeutic agent for electrophoretic distribution. (*b*) Components of the electrode.

produced by gas bubbles undergoing dielectric transport in the filter paper. The gas bubbles can be seen microscopically in a transparent medium. It is apparent that the gas production at the electrodes will disturb the ECT process by separation of the electrodes from the electrolyte. A decreasing flow of current during Phase I of ECT with oscillations of the voltage is often experienced as pain by the patient and is caused by production of gas bubbles leaving the electrodes. This drawback can be counteracted by flushing the electrode with for instance saline solution which represents one of the useful functions of the Superflux® electrodes (Fig. 7).

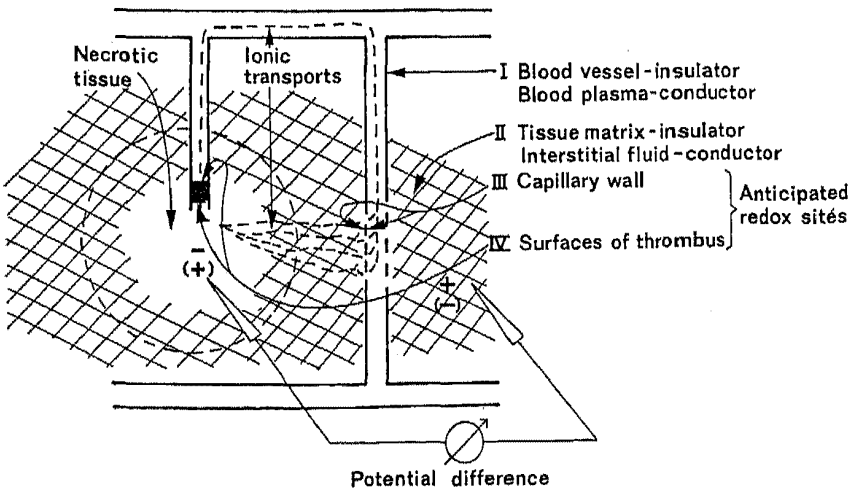


Fig. 8. The VICC system. Veins and arteries are relatively insulating the conductive blood plasma. They can therefore function as "cables" for ionic current. Capillaries "leak", i.e. they are electrically connected to the blood plasma. Necrosis leads to a fluctuating injury potential of cancer/peripheral tissue. Normally metabolic potential differences drive the VICC system. The voltage difference drives the ions in the VICC.

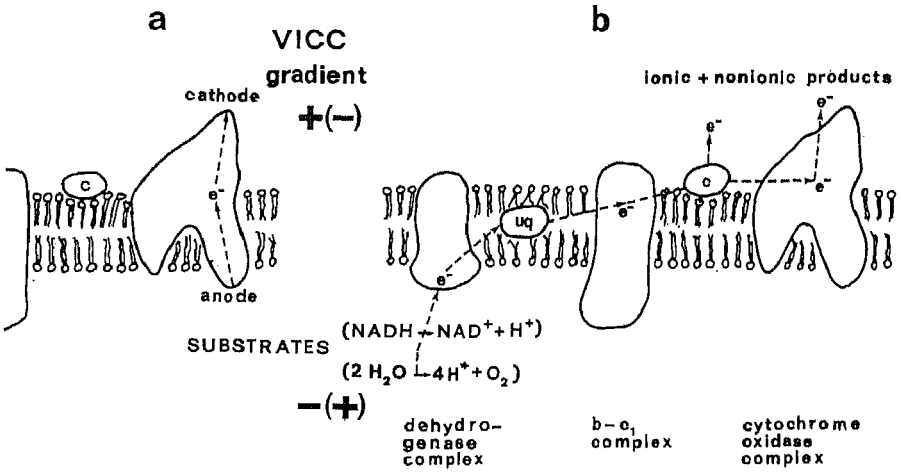


Fig. 9. Oxyreductases in a cellular wall with the capacity to transmit electrons. These are subjected to co-transport in the superimposed field gradient, the driving force. It fluctuates in the VICC circuit giving rise to reversible redox reactions. It is suggested that the flow of electrons either proceed directly (*a*) or indirectly (*b*) along the major respiratory enzyme complexes (dehydrogenase, b-c complex and oxidase complex) to the ultimate electron acceptor, oxygen.

It is commonly but falsely believed that the H^+ and OH^- ions and other products of the electrode-electrolyte-contact reactions are exclusively responsible for all the effects of the ECT (compare Galvanic "contact current"). The situation is considerably more complex, however, due to a multitude of mechanisms connected to BCEC which lead to the structural and functional effects of the distant field ("DF-effects") concept.

VASCULAR AND INTERSTITIAL GUIDANCE

In order to understand the DF effects a survey is here presented of the construction of the specific type of BCEC circuit we deal with in ECT: the vascular-interstitial closed circuit (VICC).

The VICC corresponds to the technical circuitry of Fig. 1 and represents the *in vivo* nutritional channels of all tissues, including cancers. This is possible because the circuit consists of nutrient conductive loops formed by arteries and veins (Fig. 8). These have a 200 times higher insulating property of their walls as compared with that of the conducting blood plasma. Arteries and veins therefore form conducting "cables" which are also electrically connected over the capillaries with the interstitial fluid, conductive as the blood plasma. Necrosis in a cancer gives an "injury-potential" (9). Usually, the VICC is activated by metabolic polarisation.

It is, however, not sufficient for a VICC to function only with ionic conduction in loops and the presence of a voltage gradient. Electrode-electrolyte reactions are always required in any electrophoretic process. This function is possible in the VICC system because biological electrodes (Fig. 9) exist in the walls of for instance all endothelial capillaries (9, p. 134) as oxyreductases (globular proteins with redox functions) (2, 10, 11).

The occurrence of redox reactions *in vivo* are disclosed by the formation of nonionic molecules which, in contrast to the created ions, are contracting. This leads to structures such as vesicles, observable at electron microscopy. A macroscopical analogue to this is shown in Fig. 10*a–c*. In Fig. 10*d* a drawing by Elfvin is shown of the synaptic vesicles (3). In this context, the proposed formation of for instance synaptic vesicles is a result of endogenous production of nonionic material via the action of redox enzymes, might also constitute the background of the endocytotic transformation of materials such as lipids.

A switching system for the activation of these biological, reversible electrodes also exists (9, p. 137). The switching mechanism has its target positioned on the outer walls of arterial capillaries of all mammals (except the smallest mammal, the shrew). It consists of segmentally located pericytes (Fig. 11*a–c*). These cells (12) (Fig. 12), with long extensions ("arms") and short extensions ("fingers") function as mediators of electropositive and electronegative fields (9, pp. 136–142). At *in vivo* microscopy it can be observed that the application of a superimposed field over the capillaries produce segmental contractions of arterial but not

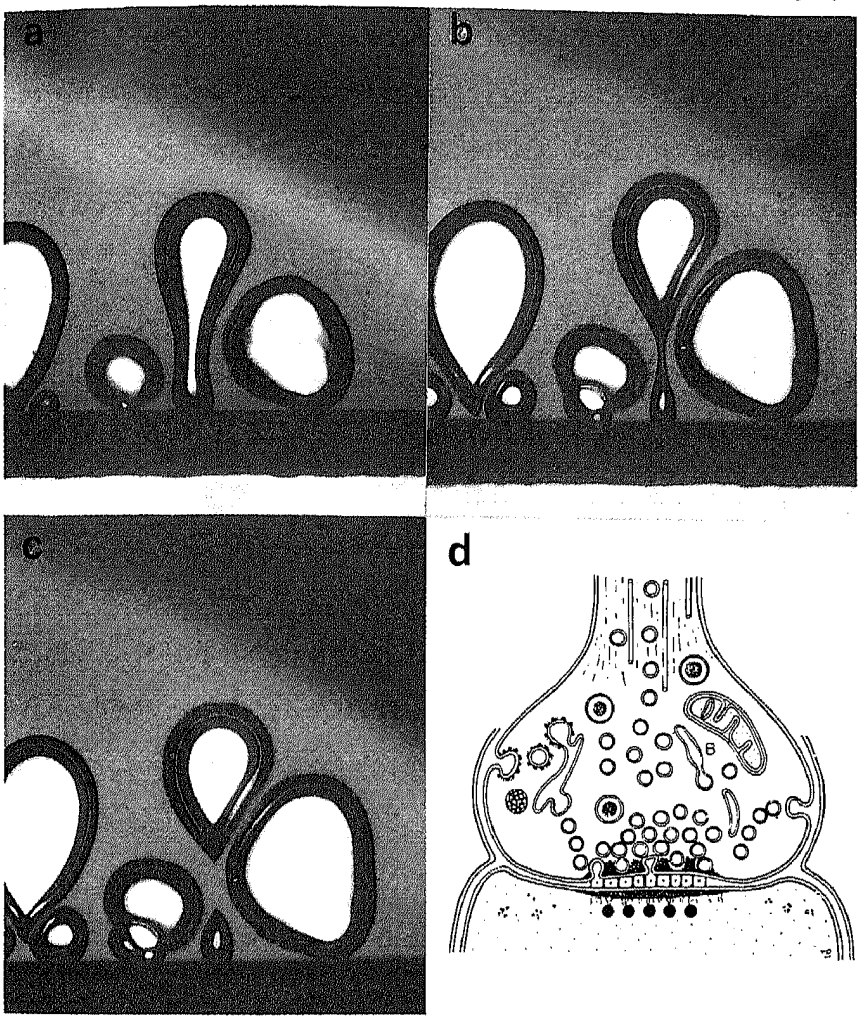


Fig. 10. Experimental analogue to the development of "vesicles" at the anodic platinum electrode in blood. The double contoured "bilateral bags" are nonionic material of contracting gas molecules (*a–c*) which may be compared with vesicles at the synaptic membranes (*d*) according to Elfvin (3).

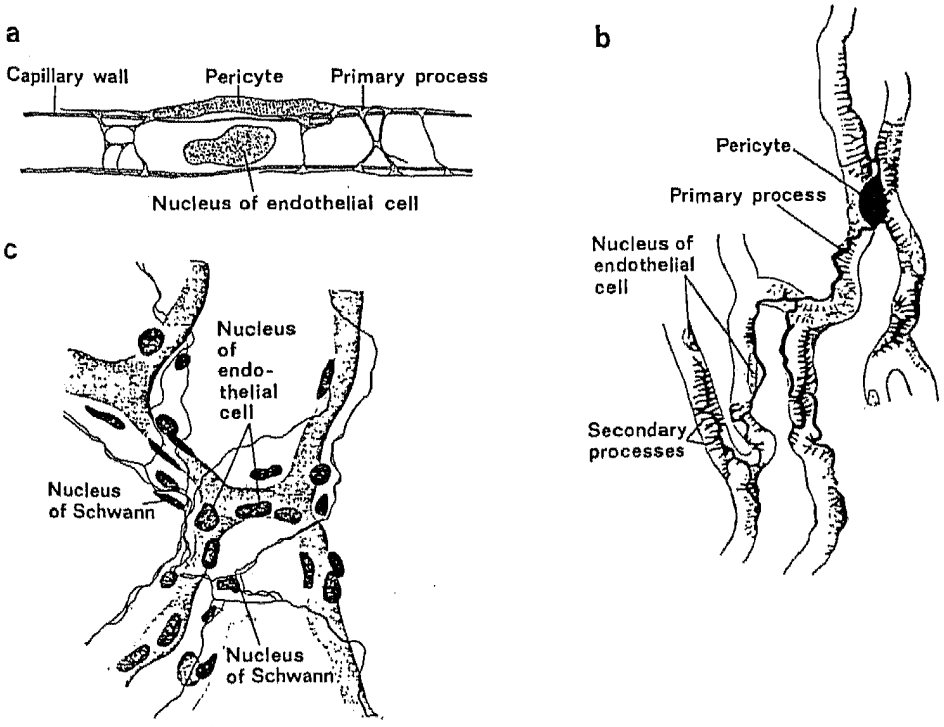


Fig. 11. (*a–c*) The pericytes are located on the outer wall of arterial endothelial capillaries. When exposed to an electromagnetic field they seem to mediate the induction of segmental contraction of the arterial but not venous capillaries.

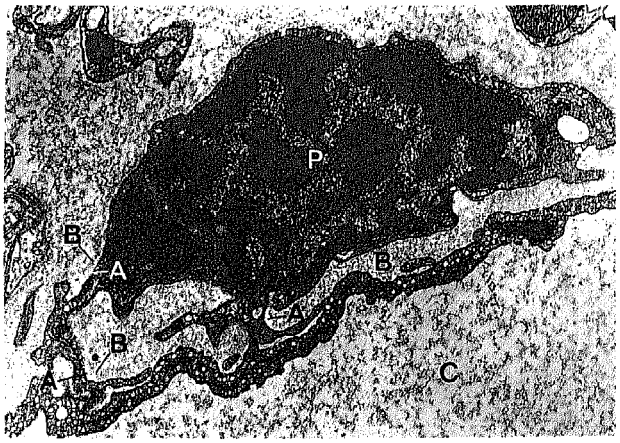


Fig. 12. A pericyte (P), electron microscopy by Weibel (12).

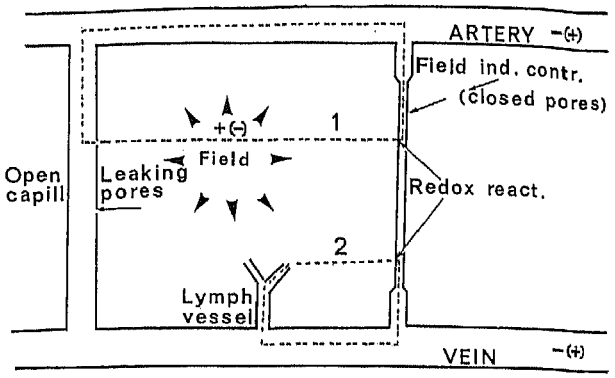


Fig. 14. Survey of induction of electrophoresis over a VICC. The segmental contraction closes ionic transports via arterial capillaries but not electron transfer.

venous capillaries (Fig. 13*a–b*). The contracted part of the arterial capillaries become very narrow. They do not leave passage for blood cells but still contain a lumen with conductive plasma. These contractions do not seem to permit ions to pass the "leaking pores"

Fig. 13. Dog mesentery, *in vivo* microscopy with subsequent excision and staining the unsectioned material (Htx-eosin). Section of a contracted capillary artery without blood cells can be seen adjacent to a non-contracted venous capillary with blue stained granulocytes. (*a*) Survey, (*b*) Detail.

or stomata between the endothelial cells. On the other hand, in the gradient of the field, electrons are transferred via the redox enzymes through the endothelial cellular walls (Fig. 15) combined with intracellular ionic transport. The negative ions and white blood cells in the non-contracted venous capillaries are thereby electrophoretically shunted from blood to interstitial tissue in the applied gradient via open "leaking" pores between endothelial cells of venous capillaries (Fig. 16).

The venous, capillary pores are even large enough to let white blood cells "crawl" by dipole induction of their cellular membranes accompanied by flow of the field induced ionic displacement in their cytoplasm into the extracapillary tissue spaces. This mechanism proposed for the "diapedesis" is shown in Fig. 16*a–c*. Similar transports also occur with red blood cells in diapedetic bleedings (9, pp. 138–141).

DISTANT FIELD EFFECTS ("DF EFFECTS")

The circulating electromagnetic field is the basis of induction of all electrically derived interactions in the tissues. The most intense local reactions occur at the electrode-electrolyte interphases which we take advantage of for the "primary" destruction ("killing") of a diagnosed cancer. The field, circulating in the tissues outside the cancer, also induces interactions with the biological substrate all the way between the electrodes. But these effects are considerably more complex and superficially less apparent than the "primary" electrode-electrolyte reactions. In fact, these effects, which are here called "distant field effects", are of considerable importance and interest but unfortunately as yet only partly understood. Examples of such "DF effects" will be given below.

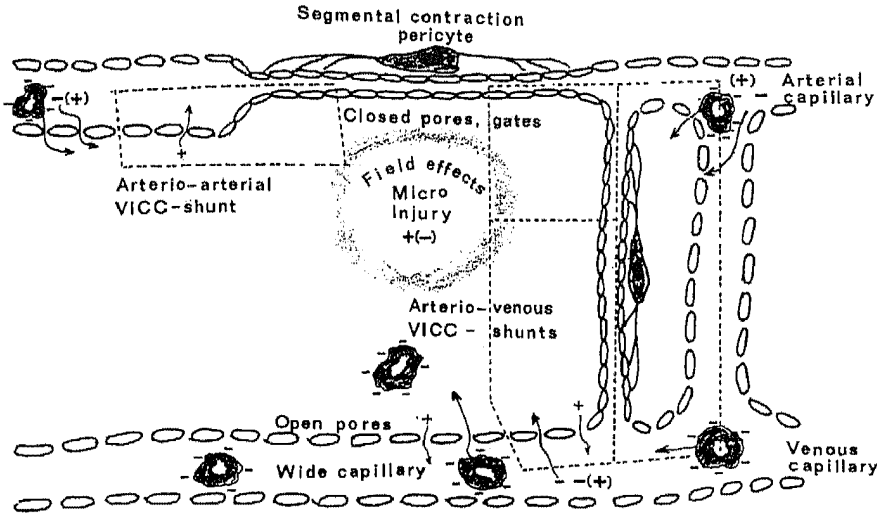
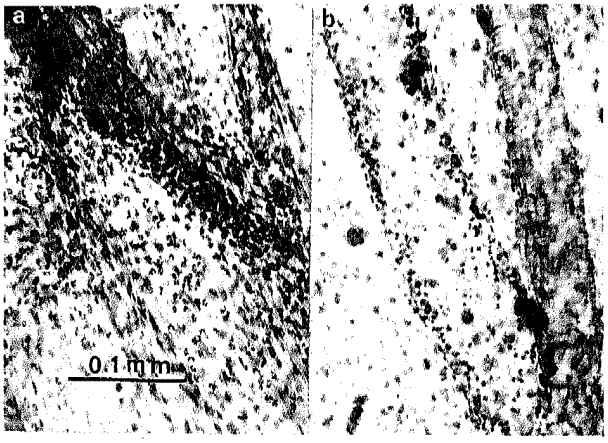


Fig. 15. In the gradient, ions and cells with surplus of electronegative charge are shunted via open leaking pores between endothelial cells of venous capillaries into the tissue.

RESTRUCTURING OF TISSUE AS A RESULT OF DF

One example of transformation of tissue is the development of corona structures by the electric field around an injury-polarised, centrally necrotic cancer (9, pp. 14–44). Edge enhancement, at irregular protrusions of the tumour surfaces produced by dipole induction in dielectric debris from cellular membranes, etc., will result in radiating structures as well as electro-osmosis, seen as a dehydrated "A"-zone and a hydrated "B" zone (Fig. 17). In total, 13 various structural modifications are already identified in the corona complex (9, Chapter III).



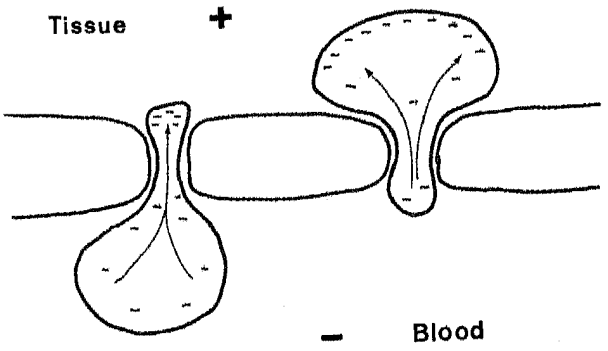


Fig. 16 (*a*, *b*) In the gradient across the endothelial venous capillary leukocytes show layering at the capillary walls. (*c*) The leukocytes then "crawl" through narrow endothelial pores (stomata) by dipole induction in the walls and ionic displacement inside the cells.

Fig. 17. Expressions of DF effects around a cancer with central necrosis (injury polarisation) are represented by the corona structures. Such are seen as radiating structures and an "A"- and a "B"-zone around this tumour.

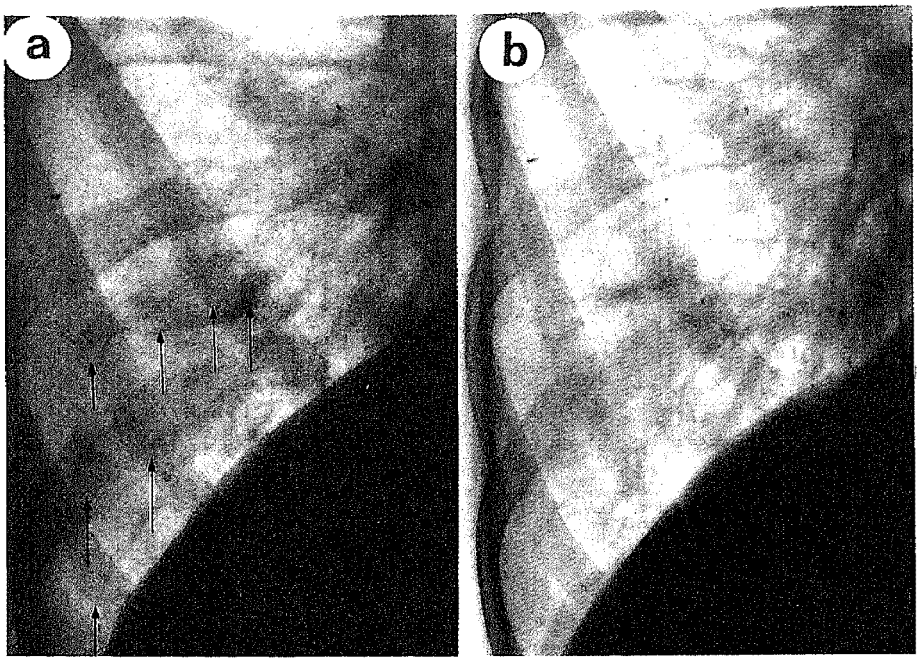


Fig. 18. Distant field (DF) effects. Woman with multiple small metastases in the right lung (*a*, *arrows*) from a pelvic sarcoma. After ECT of two larger tumours in the lung, one was given 100 C at 10 V and the other 180 C at 10 V with the tumours anodic. The small tumour metastases had disappeared four months later (*b*).

DF EFFECTS OBSERVED ON PULMONARY METASTASES

Of particular interest are the disappearance of local islands of metastatic cells which from time to time can be observed in the lung in connection with ECT of a larger "primary" tumour in the lung.

Small metastases from a previously operated pelvic sarcoma of a 60-year-old woman (9) can be seen in the lower lobe of the right lung shown in Fig. 18*a*. After ECT of two "primary" tumours in the lower lobe the small metastases in the lung regressed partly or completely (Fig. 18*b*). The small metastases were located far away from the electrodes and no other treatment had been given.

It is unlikely that the products of electrode reactions should have caused the regression of the metastases shown in Fig. 18*b*. Therefore another explanation should be sought. It is suggested that there are certain mechanisms related to the DF effects which each or in combination give a plausible explanation.

TUMOUR REGRESSION BY DEVELOPMENT OF MICROTHROMBOSIS AS A RESULT OF DF

In the "central destruction area" of the anode the dark material of acidic haematin corresponds to scattered locations of diapedetic bleedings far out in the electric field (Fig. 19*a–b*). They later on turn brown to dark-brown. The field circulation will, as an explanation, activate multiple sites of electron transfer in the distant field via the endothelial redox proteins. Reaction products will be produced leading to destruction of

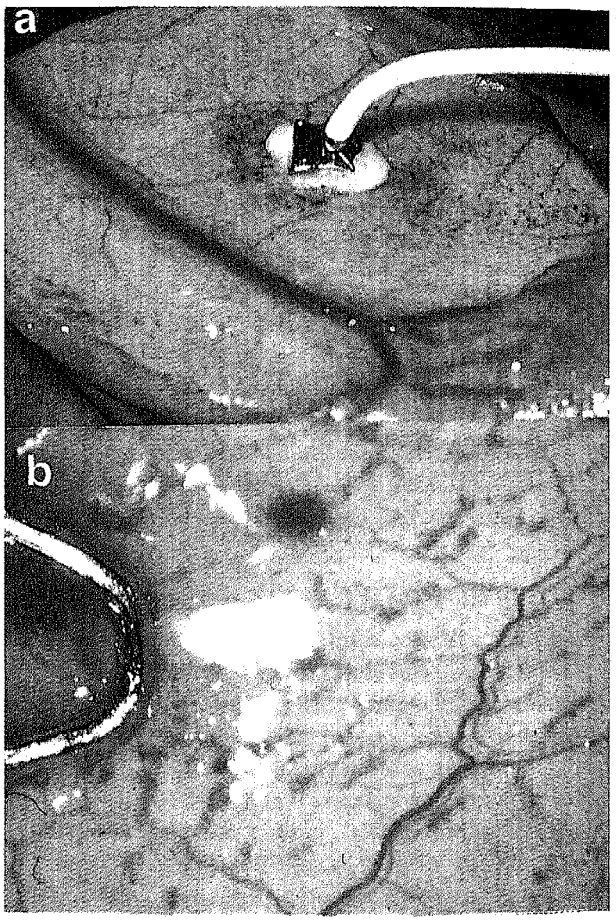


Fig. 19. (*a*) Mesentery in living dog. In the distant field, multiple small diapedetic bleedings are induced between anode at mesentery and cathode in aorta. The activation of the switching mechanism in the arterial capillaries will lead to anodic acidity transferring blood haematin into acidic haematin which appears as brown spots. (*b*) Detail of diapedetic bleedings.

Fig. 20. Field induced blockings of precapillary arterial vessels lead to permanent suspension of vascular supply to larger regions where small metastases may be localised.

the blood and formation of multiple capillary microthromboses (Fig. 20). It is likely that the location of malignant cells in an area with suspended capillary blood circulation will lead to regression or extinction of the malignant cells.

ELECTRO-OSMOSIS, DIELECTRIC TRANSPORTS

Electro-osmosis is a particularly important effect of DF. The mechanisms involved depend on the presence of a matrix with narrow interstitial "capillaries". These are known to be provided with a surplus of fixed electronegative charges in the walls of closed circuit electrophoretic VICC channels. Further, the VICC system must be activated by a voltage gradient (9, Chapter IX). The endogenous VICC channels are powered by either metabolic or injury processes or may be powered artificially between implanted electrodes (in ECT). *In vivo* tissue water always flows electro-osmotically from anode to cathode. In Fig. 2*d* it was shown that even pencil-wide pulmonary arteries in the dog were narrowed, forming obstructing funnels by an electro-osmotic increase of tissue turgor pressure in the cathodic field. This means that also the capillaries in the cathodic field have a completely suspended circulation (while the microthromboses block the capillaries in the anodic field).

In Fig. 21*a* the right lower lobe is shown radiographically in a woman with one electrode (anode) in a fibro-lipo-sarcoma metastasis and one electrode (cathode) about 8 cm medially of the tumour in the right lower lobe. After 250 C at 100 V a dense region of electro-osmotic water is collected around the cathode due to electro-osmotic tissue water (Fig. 21*b*).

Cancer tissue is often more sensitive than normal tissue to chemotherapeutics, heat, cold, and radiation. A sufficiently long time of vascular obstruction will evidently seriously interfere with the living conditions of the tissues.

These aspects focusing on transport of tissue water are also largely relevant for dielectric particles, e.g. neutral lipids. Such ECT transports can, however, only be predicted on the basis of actual field strengths, of molecular size of particles in relation to capillarity, and surface charge of the tissue matrix.

FIELD-INDUCED CASCADE DISINTEGRATION OF NEOPLASTIC TISSUE

The ionic separations by the circulating field are evi-

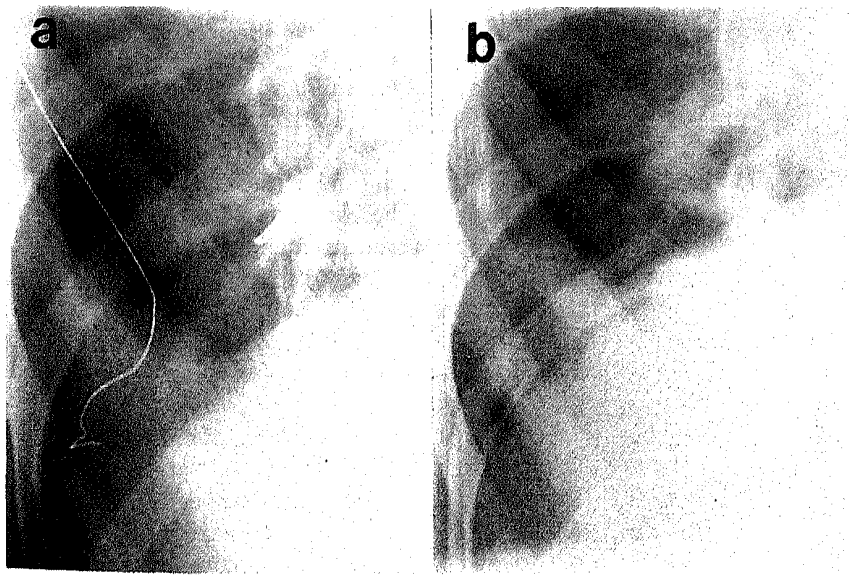


Fig. 21. (*a*) Before treatment of human fibroliposarcoma. (*b*) 250 C at 10 V were given between the anode in the tumour and the cathode (right). The dense region around the cathode after the treatment is caused by electro-osmotic flow of tissue water.

dent in an electrolyte. The induction of ionic and dielectric transports also occur in semi-solid conducting media.

Electrophoretically induced sequential or cascade reactions, well known from chemistry, may at least theoretically be considered as a possible mechanism underlying the induction of intracellular disintegration of (neoplastic) tissue. Such reactions are known to occur at the formation of for instance intravascular thrombosis (Fig. 22). They may also start

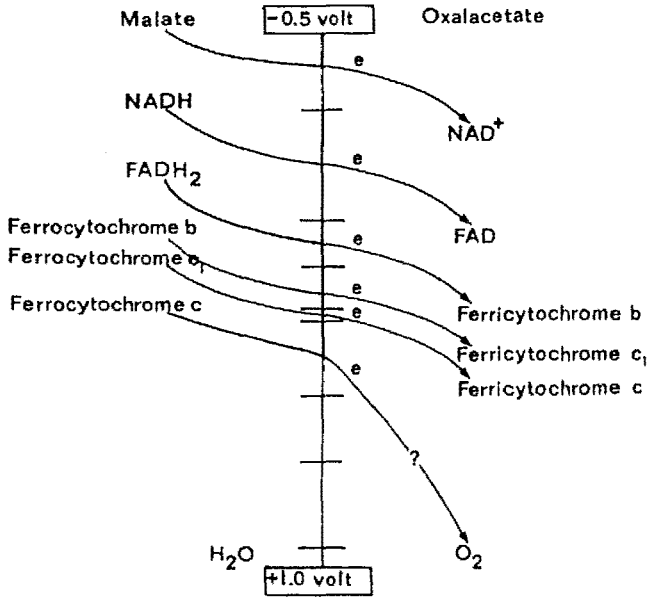


Fig. 22. Cascade reactions at the degradation of blood leading to thrombosis (according to Jordan). Note that one reaction leads to favourable conditions for a following reaction. As a result, an overall 1.5 V voltage change takes place.

with development of cytoplastic structuring and transition of material into new birefringent material (Fig. 23*a*), crenations and polychromasia (Fig. 23*b*), central concentration of materials (Fig. 23*c*), and vacuoles (Fig. 23*d*). These changes were produced in human blood at 6 V after 0.005 C of flow of direct current. Further evidence of such mechanisms has been given previously (9, Chapter XVI).

In Fig. 24*a* a metastasis from breast cancer in an 82-year-old woman is seen. After ECT with one platinum string electrode (anode) in the tumour and another (cathode) 3 cm above the tumour, 100 C were given at 10 V. The tumour disappeared gradually over about one month without leaving any residual injured (scar) tissue (Fig. 24*b*), which may indicate selective tumour regression (disintegration of malignant cells).

FIELD ACTIVATION OF THE IMMUNOLOGICAL SYSTEM

At ECT, the anodic field will attract white blood cells which are known to be electronegatively charged (13). In Fig. 25, an electrode is seen placed on the mesentery of a living dog and the cathode in the aorta. Already at 1 V overpotential (0.002 C) the mesentery was excised and stained (Fig. 25*a* is an overview, Fig. 25*b* shows an enlarged section). The field-induced contraction of the arterial capillary is empty of cells, but the venous precapillary contains an abundance of blue-stained granulocytes (Htx-eosin).

By making the mesenteric electrode electronegative, the field will repel the electronegative white blood cells. When they flow in veins directed towards the cathode a field-flow interference will occur, leading to accumulation of white blood cells, as seen in Fig. 26.

The observations show that local accumulation of charged white blood cells is electrophoretically transported in the applied field. This may also indicate that spontaneous so-called leukotaxis might be explained energetically as an *in vivo* electrophoresis of the VICC system.

The *in vivo* accumulations of leukocytes to the anodic tissue region also seem to indicate that a field-induced activation of the immunological system, with high probability, is induced at ECT.

Various immunomodulators, activating macrophages with the ability selectively to destroy neoplastic cells are also believed to be put into action by the electrophoretic ECT flow of current. After endocyte formation of liposomes containing immunomodulators, generating cytoaggressive macrophages, the targeting should be provided by the ECT current. Works by Fiedler (4), Hauton (5–8), and others indicate that future treatment of metastases should proceed along these lines.

The Superflux electrode (Fig. 8) is provided with a canal for flushing the electrode. A charged agent such as the electropositive adriamycin or the electronegative 5-fluoracil can be infused into the electrode. When charging the electrode with equal polarity as the agent, an even distribution of the drug with high concentration can lead to remarkable regression and palliative effects of even large, incurable cancers. Supplied intravenously or orally, these two agents are attracted to the electrode, when given opposite polarity.

Fig. 27*a* shows a large squamous cell carcinoma in the right upper lobe of a 70-year-old man. One Superflux electrode was inserted percutaneously into the tumour centre under local anaesthesia. Fifty mg of adriamycin was slowly infused under application of

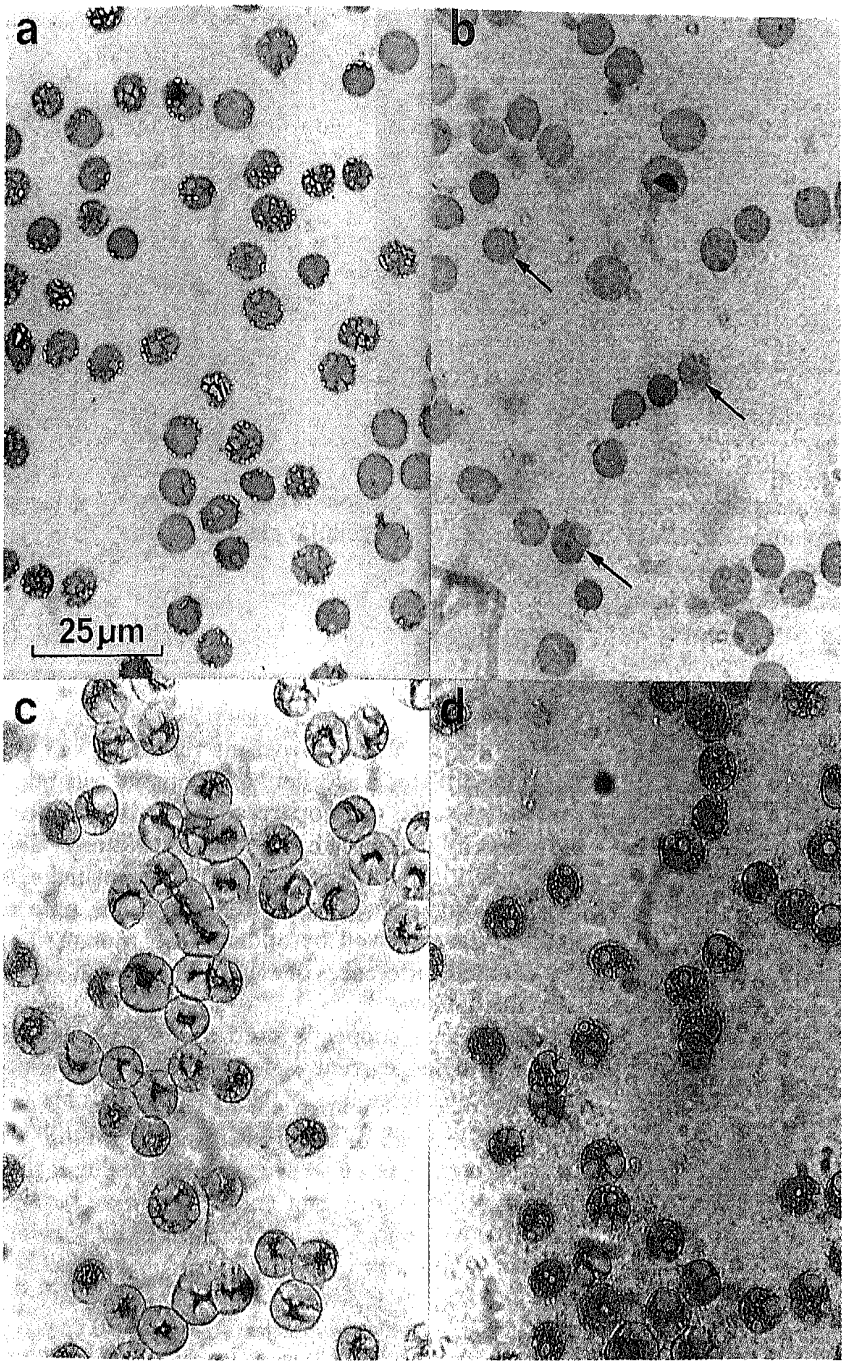


Fig. 23. Human venous blood on a glass slide is exposed to 0.005 C at 1 V overpotential between two platinum electrodes. Various structural modifications occur in the anodic area. (*a*) Birefringent particles and (*b*) crenations and polychomasia. In the cathodic field (*c*) "spokes in wheels" and (*d*) vacuoles are formed.

+10 V in relation to a platinum electrode in the subcutis of the suprajugular fossa. The result of this palliative treatment six months later is seen in Fig. 27*b*. The easily provided ECT with enhancement of the destructive effects of adriamycin had by then produced a palliative treatment, because one year later the tumour started to grow again.

ELECTROMAGNETIC HOMOEOSTASIS (EMH): INFLUENCE OF DF EFFECTS IN ECT

It has constantly been found that the flow of electricity in tissue leads to various modifications of cells and tissues (9).

With our present knowledge of electricity it is evident that the flow of ions in the BCEC channels leads to the development of electromagnetic fields. These constitute an important part of the biological microenvironment of tissue and cells and should be looked upon in terms of electromagnetic homoeostasis (EMH). A section of a modified normal flow of ions in blood, vessels, interstitial, or other BCEC channels will lead to a disturbance of the EMH. The super-

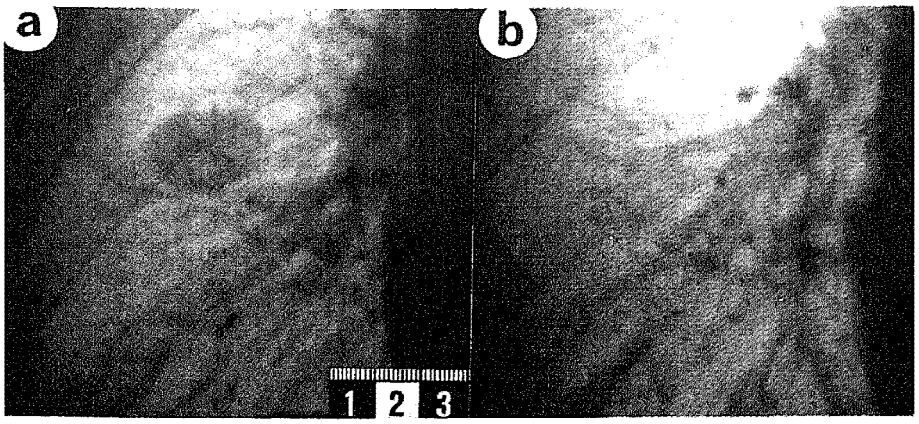


Fig. 24. (*a*) Mammary breast cancer metastasis in a 82-year-old woman. After delivery of 100 C at 10 V (the tumour anodic, the cathode positioned 3 cm above the tumour) the tumour disappeared after four months. No structural changes are seen in the lung.

imposition of current (e.g. ECT) or externally moving electromagnetic fields will equally change the EMH in addition to the appearance of abnormal eddy currents in the cellular cytoplasm which may alter both structure and function. This was possibly a factor contributing to the cellular changes illustrated in Fig. 23.

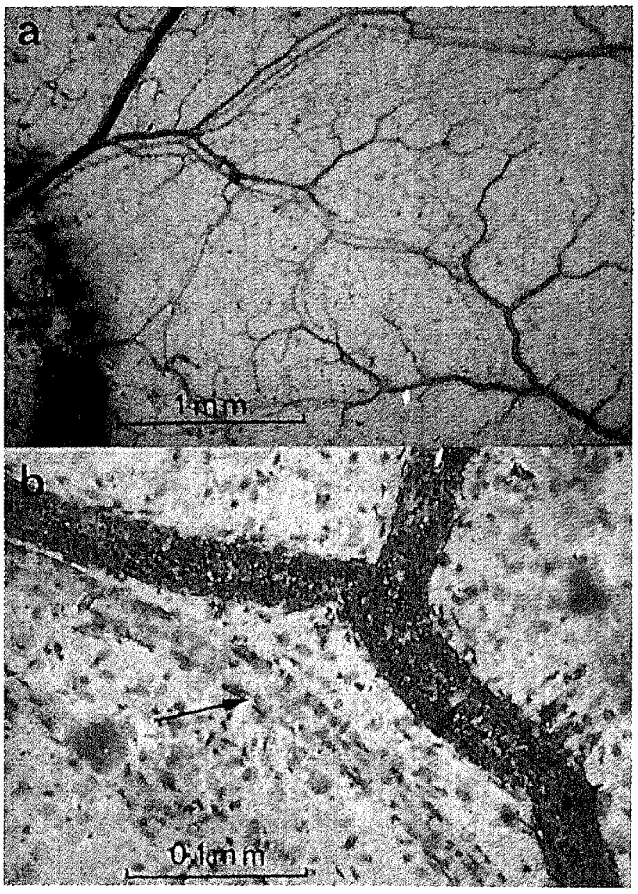


Fig. 25. Dog mesentery. Electrode (anode) placed on the mesentery and the cathode in the aorta. After 0.002 C, 1 V overpotential, white blood cells accumulated in veins. Arterial capillaries segmentally contracted [(*a*) is an overview, (*b*) microscopic enlargement] (Htx-eosin). Dark cells in the veins are leukocytes. Note the empty contracted arterial capillary (*arrow*).

ELECTRODES

Platinum as a metal is stable for most anodic and cathodic electrochemical reactions. Its catalytic power, i.e. its ability to permit reactions with the tissue electrolytes is excellent as compared with other metals. It also has the property of enhancing the speed of reactions when increasing the overvoltage, also here superior to other metals. However, platinum is expensive and rather brittle. The mechanical properties can be improved by adding 10% iridium. The considerable differences of electrodic material will be described below.

Assume that copper is used as both anode and cathode. When current is led between these electrodes in an electrolyte of NaCl in water, only the cathode will show formation of gas bubbles. Litmus

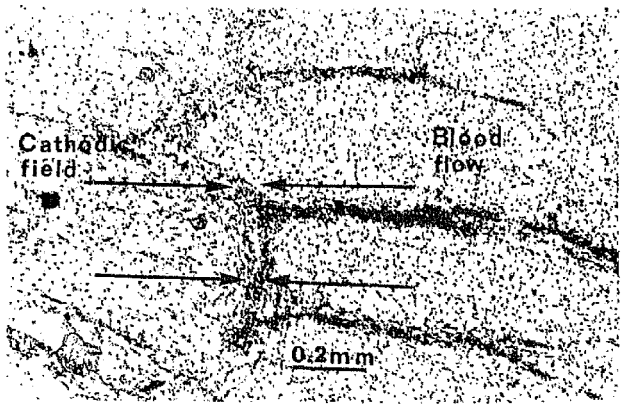


Fig. 26. A negative field directed opposite the flow of veins will lead to gradual accumulation of negatively charged particles and white blood cells. The latter are here seen as dark particles in mesenterial veins and present an example of field-flow interference.

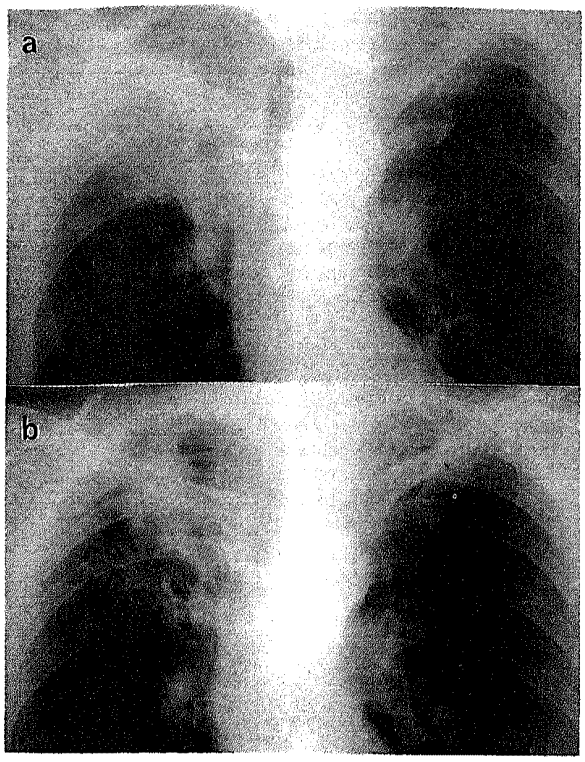


Fig. 27. (*a*) Male, 70 years, squamous cell carcinoma with mediastinal growth before treatment. Palliative treatment with one Superflux electrode introduced percutaneously into the center of the tumour and one electrode into the subcutis of the suprajugular fossa. Infusion of 50 mg of adriamycin (electropositive) into the electrode canal with application of 10 V direct current, anode positive. (*b*) The reduction of the tumour six months later.

paper will be blue in the cathodic region but there will not be any acidic reaction in the anodic region. This is due to the corrosive characteristics of copper. Sodium ions will migrate and diffuse to the cathode and accept electrons to become sodium atoms. These will decompose water with development of hydrogen gas and produce sodium hydroxide which dissolves in water. The hydroxyl ions give the base reaction. The chlorine ions reach the anode and donate their negative charge to the anode, which corrodes, i.e. gives off copper ions, forming copper-chloride, which dissolves in water. There will not be any production of acidity or gas. If platinum is used as the material of the anode, the chlorine ions decompose water forming O_2 and hydrochloric acid. An advantage with platinum is that it will not corrode.

The electrodes should present a large surface area but be easily introducible into tissue without producing too much damage. The most efficient electrodes produced so far are the coils of platinum (Superflux electrodes®) which are easily implanted. Through this electrode it is possible to infuse for instance saline solution for removal of gas and for injection of other agents such as chemotherapeutics.

The anode and cathode should have equal surface areas so that the cathode at least will not produce a limiting step for the flow of current.

Regression of cancer tissue can take place both around the anode (+) and the cathode (−) in the tumour. It may therefore seem logical to place both anode and cathode in the cancer. Such a positioning of electrodes can, if a sufficient dose of current is given to a T_1 tumour, lead to a treatment result comparable with an initially successful surgical removal of a cancer. Not seldom after surgical removal of the tumour, metastases may, after some time, start growing in the tissue around the former place of the tumour. They may have developed as local metastases in the surrounding tissue of the cancer, but have remained undiagnosed at the time of surgery. This kind of peripheral recurrence may also have taken place before local ECT extinction of a cancer with anode and cathode in the tumour. To be able to utilize the DF effect described, the anode and cathode should be positioned far away from each other to create a large field. Thereby a better effect may be expected as compared with local surgical removal, or ECT with closely positioned electrodes. These aspects are important and may indicate that ECT of "small resectable" cancers might be more efficient than conventional surgical resection.

Electrodes positioned very closely to each other will give a relatively small electric field and the risk for a "linear breakthrough" of current is evident. This also obviates the risk of relatively insufficient diffusion and migration of toxic products caused by local electrode reactions.

The latter drawbacks also exist when several anodes and cathodes are used. An uneven distribution of current will occur between pairs of anodes and cathodes as they will present differences of internal resistances in the conductive fluid of the cancer. In addition, field interferences will occur.

By positioning anodic and cathodic electrodes far from each other the dose requirements for treatment will be hampered by a lowering of the flow of current, which has to be compensated for by a longer time of treatment or improvement of the electrodes. The risk of injuring sensitive tissue also requires special attention.

Upon this background it may be evident that a sufficient dose of treatment should be given during Phase I. The electropositive polarity during Phase I will efficiently keep malignant, electronegatively charged cells attached to the anodic tumour. The cells should preferably be devitalised before conclusion of

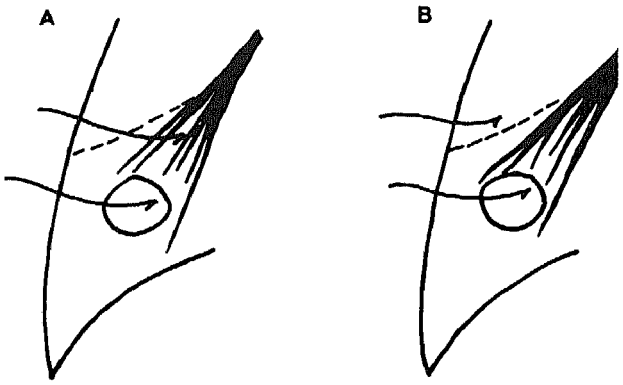


Fig. 28. (*a*) Correct positioning of electrodes in a tumour and the second electrode in the same lung lobe. (*b*). Cathodic electrode in a wrong position in the lung with interposition of a pleural sheet. Current will flow via one electrode first to the mediastinum and then to the second electrode which inherits a large risk for injury on nerves etc. in the mediastinum.

Phase I as the cancer will become cathodic during Phase II.

PRECAUTIONS AT THE POSITIONING OF ELECTRODES IN ECT

Wrong positioning of the electrodes should be avoided so that the flow of current will never injure sensitive tissue. In Fig. 28*a* an electrode is schematically inserted into a tumour in the middle lobe of the right lung. The other electrode is also positioned in the middle lobe, which will allow current to pass in a correct way. In Fig. 28*b* the second electrode is positioned at an equal distance from the tumour electrode, but in an incorrect way. The interlobar pleura will, by its electrical resistance, force the current first to pass into the mediastinum and then out to the tumour electrode. With this incorrect positioning of the second electrode it is likely that for instance the nerves in the mediastinum will be seriously injured. This is valid of any organ in the body.

Also the electromagnetic field can cause serious damage due to incorrect electrode positioning. A venous catheter passed via the right atrium and ventricle to the pulmonary artery or its branches cannot be used for introduction of an electrode into the lung (see Fig. 2 from a lung experiment). The flow of current through the catheter-electrode will create an electromagnetic field which may seriously impair the function of the heart.

Fig. 29 shows an anaesthetised dog provided with one electrode in the subcutis lateral to the left lung and the second electrode in the subcutis lateral to the liver. By using 40 V (which is too high), an almost linear "break-through" of the current occurs between the electrodes. An almost circular black core of damaged tissue developed through the skin on the left side, the underlying part of a rib, the diaphragm, the stomach, the liver, and the skin on the right side. The standard voltage to be used is 10 V in humans.

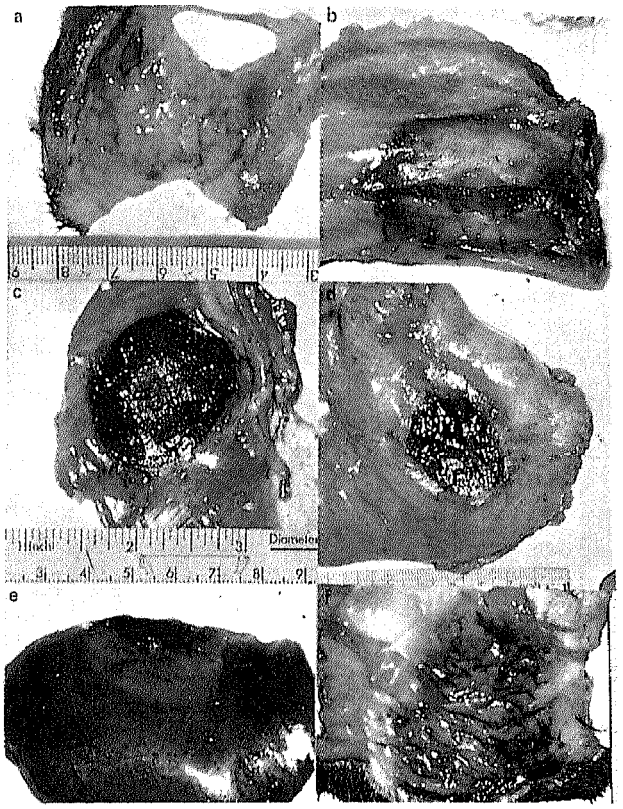


Fig. 29. Too high voltage in ECT. The current causes a "linear breakthrough" with injury to (*a*) the left chest wall, (*b*) the underlying rib, (*c*) the diaphragm, (*d*) the stomach, (*e*) the liver, and (*f*) the right chest wall.

Under no circumstances should a "reference" electrode be placed on the skin during ECT, similar to what is commonly used in diathermia, when high frequency alternating current is used. In ECT the applied direct current might choose an unpredictable way to the tumour electrode and damage vital organs such as the heart, spinal cord, and nerve stems.

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